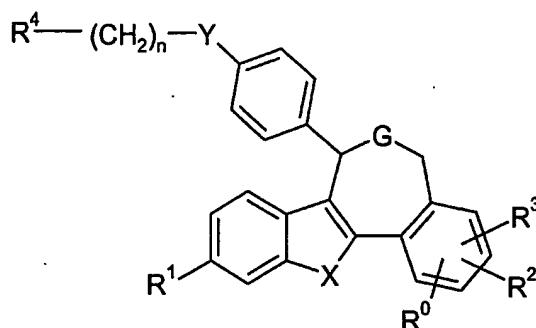


-68-

WE CLAIM:

1. A compound of the formula



(I)

wherein

R^1 is -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl), or -OSO₂(C₂-C₆ alkyl);

R^0 , R^2 and R^3 are each independently -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl), -OSO₂(C₂-C₆ alkyl) or halo;

R^4 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, diisopropylamino, or 1-hexamethyleneimino;

n is 2 or 3

X is -S- or -HC=CH-;

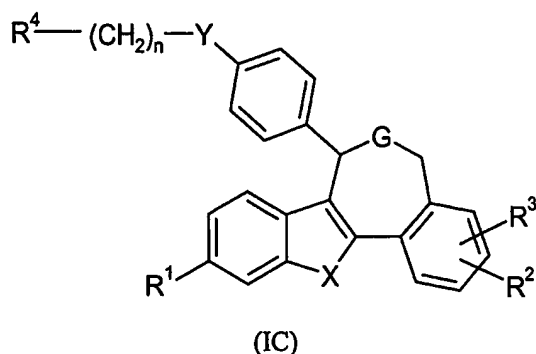
G is -O-, -S-, -SO-, SO₂, or -N(R⁵)-, wherein R⁵ is -H or C₁-C₄ alkyl; and

Y is -O-, -S-, -NH-, -NMe-, or -CH₂-;

or a pharmaceutically acceptable salt thereof.

-69-

2. A compound of Claim 1 of the formula



5 wherein

R^1 is -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl), or -OSO₂(C₂-C₆ alkyl);

R^2 and R^3 are each independently -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl), -OSO₂(C₂-C₆ alkyl) or halo;

10 R^4 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, diisopropylamino, or 1-hexamethyleneimino;

n is 2 or 3;

X is -S- or -HC=CH-;

15 G is -O-, -S-, -SO-, SO₂, or -N(R⁵)-, wherein R⁵ is -H or C₁-C₄ alkyl; and

Y is -O-, -S-, -NH-, -NMe-, or -CH₂-;

or a pharmaceutically acceptable salt thereof.

3. A compound according to Claims 1 or 2 wherein G is -O-.

20

4. A compound according to any of Claims 1 to 3 wherein Y is -O-.

5. A compound according to any of Claims 1 to 4 wherein n is 2.

25

6. A compound according to any of Claims 1 to 5 wherein R^1 is -OH or -OCH₃.

7. A compound according to any of Claims 1 to 6 wherein R^1 is $-OH$.
8. A compound according to any of Claims 1 to 7 wherein R^4 is 1-piperidinyl,
5 1-hexamethyleneimino or 1-pyrrolidinyl.
9. A compound according to any of Claims 1 to 8 wherein R^4 is 1-piperidinyl.
10. A compound according to any of Claims 1 or 3 to 9 wherein two of R^0 , R^2
10 and R^3 is $-H$.
11. A compound according to any of Claims 1 or 3 to 10 wherein two of R^0 ,
 R^2 and R^3 is $-H$ and the other is $-OH$.
12. A compound according to any of Claims 1 or 3 to 10 wherein all of R^0 , R^2
15 and R^3 are $-H$.
13. A compound according to any of Claims 1 or 3 to 9 wherein R^0 , R^2 , and R^3
are independently $-H$ or halo.
20
14. A compound according to any of Claims 1 or 3 to 8 wherein two of R^0 , R^2 ,
and R^3 are $-H$ and the other is fluoro.
15. A compound according to any of Claims 1 or 3 to 8 wherein two of R^0 , R^2 ,
25 and R^3 are fluoro and the other is $-H$.
16. A compound according to any of Claims 1 or 3 to 8 wherein R^0 , R^2 , and R^3
are all fluoro.
17. A compound according to any of Claims 1 to 16 wherein X is $-S-$.
30
18. A compound according to any of Claims 1 to 16 wherein X is $-HC=CH-$.

19. A compound according to Claim 1 selected from the group consisting of:
- 1-{2-[4-(10-methoxy-5H,7H-6-oxa-12-thia-dibenzo[a,e]azulen-7-yl)-phenoxy]-ethyl}-piperidine;
- 5 1-{2-[4-(10-methoxy-5H,7H-6-oxa-12-thia-dibenzo[a,e]azulen-7-yl)-phenoxy]-ethyl}-pyrrolidine;
- 7-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5H,7H-6-oxa-12-thia-dibenzo[a,e]azulen-10-ol;
- 7-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5H,7H-6-oxa-12-thia-dibenzo[a,e]azulen-10-ol;
- 10 1-{2-[4-(8-methoxy-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-11-yl)-phenoxy]-ethyl}-piperidine;
- 1-{2-[4-(8-methoxy-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-11-yl)-phenoxy]-ethyl}-pyrrolidine;
- 15 11-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;
- 11-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;
- 11-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalene-2,8-diol;
- 20 11-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalene-2,8-diol;
- 2-fluoro-11-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;
- 25 2-fluoro-11-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;
- 1,2-difluoro-11-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;
- 1,2-difluoro-11-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;
- 30 1,2,3-trifluoro-11-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;

1,2,3-trifluoro-11-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-
benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;

1,3-difluoro-11-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-
benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;

5 1,3-difluoro-11-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-
benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;

1-fluoro-11-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-
benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;

10 1-fluoro-11-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-
benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol;
and pharmaceutically acceptable salts thereof.

20. A compound according to Claim 1 wherein said compound is 7-[4-(2-
piperidin-1-yl-ethoxy)-phenyl]-5H,7H-6-oxa-12-thia-dibenzo[a,e]azulen-10-ol; or a
15 pharmaceutically acceptable salt thereof.

21. A compound according to Claim 1 wherein said compound is 11-[4-(2-
Piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-
a]naphthalen-8-ol; or a pharmaceutically acceptable salt thereof.

20

22. A compound according to Claim 1 wherein said compound is 11-[4-(2-
piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-
a]naphthalene-2,8-diol; or a pharmaceutically acceptable salt thereof.

25 23. A compound according to Claim 1 wherein said compound is 2-fluoro-11-[4-
(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-
a]naphthalen-8-ol; or a pharmaceutically acceptable salt thereof.

24. A compound according to Claim 1 wherein said compound is 2-fluoro-11-[4-
30 (2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-
a]naphthalen-8-ol; or a pharmaceutically acceptable salt thereof.

25. A compound according to Claim 1 wherein said compound is 1,2-difluoro-11-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol; or a pharmaceutically acceptable salt thereof.

5 26. A compound according to Claim 1 wherein said compound is 1,2,3-trifluoro-11-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol; or a pharmaceutically acceptable salt thereof.

10 27. A compound according to Claim 1 wherein said compound is 1,3-difluoro-11-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol; or a pharmaceutically acceptable salt thereof.

15 28. A compound according to Claim 1 wherein said compound is 1-fluoro-11-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-11,13-dihydro-12-oxa-benzo[3,4]cyclohepta[1,2-a]naphthalen-8-ol, or a pharmaceutically acceptable salt thereof.

20 29. A pharmaceutical composition comprising a compound according to any of Claims 1 to 28 or a pharmaceutically acceptable salt thereof, and optionally an effective amount of estrogen and progestin, in combination with a pharmaceutically acceptable salt, diluent, or excipient.

25 30. A method for inhibiting a disease associated with estrogen deprivation comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to any one of Claims 1 to 28.

31. A method according to Claim 30 wherein said patient is a human.

32. A method according to Claim 31 wherein said patient is a postmenopausal woman.

30 33. A method according to any of Claims 30 through 32 wherein said disease associated with estrogen deprivation is bone loss.

-74-

34. A method according to any of Claims 30 through 32 wherein said disease associated with estrogen deprivation is cardiovascular disease.

5 35. A method for inhibiting a disease associated with an aberrant physiological response to endogenous estrogen comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to any one of Claims 1 through 28.

10 36. A method according to Claim 35 wherein said patient is a human.

37. A method according to Claim 36 wherein said patient is a postmenopausal female.

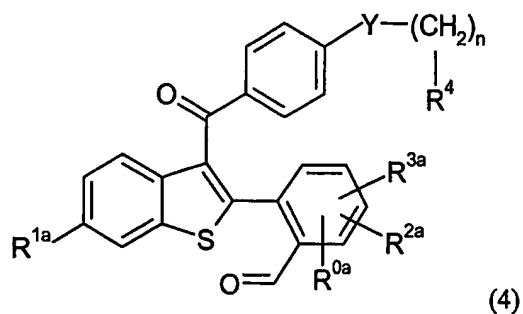
15 38. A method according to any of Claims 35 through 37 wherein the disease associated with an aberrant physiological response to endogenous estrogen is estrogen dependent cancer.

39. A method according to Claim 38 wherein said cancer is breast cancer.

20 40. A method according to any of Claims 35 through 37 wherein the disease associated with an aberrant physiological response to endogenous estrogen is endometriosis.

25 41. A method according to any of Claims 35 through 37 wherein the disease associated with an aberrant physiological response to endogenous estrogen is uterine fibrosis.

42. A compound of the formula



5 wherein

R^{1a} is -H or -OPg, wherein Pg is a hydroxy protecting group;

R^{0a} , R^{2a} and R^{3a} are each independently R^{1a} or halo;

R^4 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, diisopropylamino, or 1-

10 hexamethyleneimino;

n is 2 or 3; and

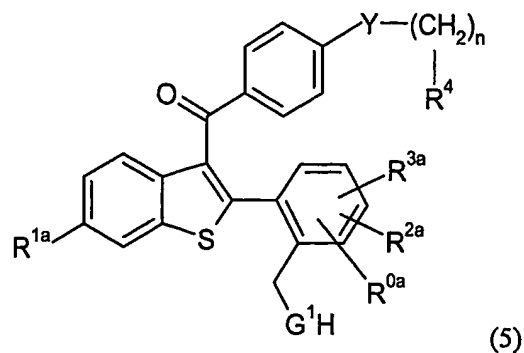
Y is -O-, -S-, -NH-, -NMe-, or -CH₂-;

or a pharmaceutically acceptable salt thereof.

15 43. A compound according to Claim 42 wherein said compound is 2-{6-methoxy-3-[4-(2-piperidin-1-yl-ethoxy)-benzoyl]-benzo[b]thiophen-2-yl}-benzaldehyde.

-76-

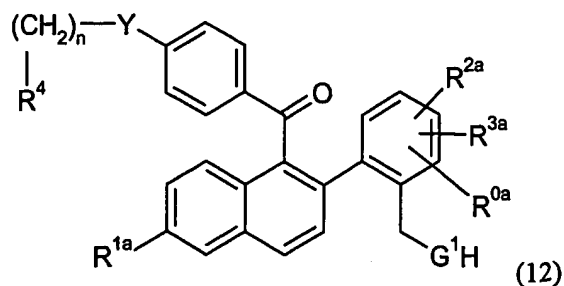
44. A compound of the formula



wherein

- 5 R^{1a} is -H or -OPg, wherein Pg is a hydroxy protecting group;
 R^{0a} , R^{2a} and R^{3a} are each independently R^{1a} or halo;
 R^4 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl,
 4-morpholino, dimethylamino, diethylamino, diisopropylamino, or 1-
 hexamethyleneimino;
 10 n is 2 or 3;
 G^1 is -O-, -S-, or -N(R^5)-, wherein R^5 is -H or C_1 - C_4 alkyl; and
 Y is -O-, -S-, -NH-, -NMe-, or -CH₂-;
 or a pharmaceutically acceptable salt thereof.

15 45. A compound of the formula



wherein

- 20 R^{1a} is -H or -OPg, wherein Pg is a hydroxy protecting group;
 R^{0a} , R^{2a} and R^{3a} are each independently R^{1a} or halo;

-77-

R^4 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, diisopropylamino, or 1-hexamethyleneimino;

n is 2 or 3;

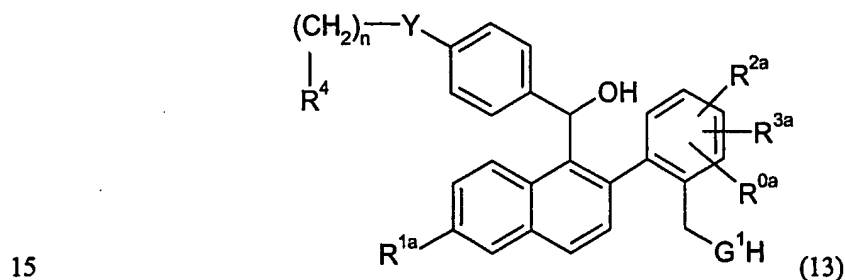
5 G^1 is -O-, -S-, or -N(R^5)-, wherein R^5 is -H or C_1 - C_4 alkyl; and

Y is -O-, -S-, -NH-, -NMe-, or -CH₂-;

or a pharmaceutically acceptable salt thereof.

46. A compound according to Claim 45 wherein said compound is [2-(2-hydroxymethyl-phenyl)-6-methoxy-naphthalen-1-yl]-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-methanone.

47. A compound of the formula



wherein

R^{1a} is -H or -OPg, wherein Pg is a hydroxy protecting group;

R^{0a} , R^{2a} and R^{3a} are each independently R^{1a} or halo;

20 R^4 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, diisopropylamino, or 1-hexamethyleneimino;

n is 2 or 3;

G^1 is -O-, -S-, or -N(R^5)-, wherein R^5 is -H or C_1 - C_4 alkyl; and

Y is -O-, -S-, -NH-, -NMe-, or -CH₂-;

25 or a pharmaceutically acceptable salt thereof.

48. A compound according to Claim 47 wherein said compound is [2-(2-hydroxymethyl-phenyl)-6-methoxy-naphthalen-1-yl]-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-methanol.

5 49. The use of a compound according to any of Claims 1 to 28 for the manufacture of a medicament for inhibiting a disease associated with estrogen deprivation.

10 50. The use according to Claim 49 wherein said disease is bone loss.

51. The use according to Claim 49 wherein said disease is cardiovascular disease.

15 52. The use of a compound according to any of Claims 1 to 28 for the manufacture of a medicament for inhibiting a disease associated with an aberrant physiological response to endogenous estrogen.

53. The use according to Claim 52 wherein said disease is estrogen dependent cancer.

20 54. The use according to Claim 53 wherein said cancer is breast cancer.

55. The use according to Claim 52 wherein the disease associated with an aberrant physiological response to endogenous estrogen is endometriosis.

25 56. The use according to Claim 52 wherein the disease associated with an aberrant physiological response to endogenous estrogen is uterine fibrosis.

30 57. A pharmaceutical composition for inhibiting a disease associated with estrogen deprivation containing as an active ingredient a compound according to any of Claims 1 to 28.

58. A pharmaceutical composition for inhibiting a disease associated with an aberrant physiological response to endogenous estrogen containing as an active ingredient a compound according to any of Claims 1 to 28.